عنوان مقاله:

Theoretical investigation of cyclooxygenase inhibition property of several non-steroidal anti-inflammatory drugs by density functional theorycalculations and molecular docking studies

محل انتشار:

فصلنامه تحقیقات جاری در داروسازی, دوره 1, شماره 4 (سال: 1394)

تعداد صفحات اصل مقاله: 12

نویسندگان:

Atena Najdian - *Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran*

Amirhossein Sakhteman - *Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran*

Maryam Mortazavi - *Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran*

Hossein Sadeghpour - *Department of Medicinal Chemistry, School of Pharmacy, Shiraz University of Medical Sciences, Shiraz, Iran*

خلاصه مقاله:

Understanding the geometry and electronic properties of non-steroidal anti-inflammatory drugs (NSAIDs) and the nature of their interactions with human cyclooxygenase-2 (COX-2) is important in the development and design of novel NSAIDs. In this paper, B3LYP/6-311++G (d,p) level of theory was appliedto assess the acidity of NSAIDs in the gas phase. Subsequently, the role of intramolecular hydrogen bond on acidity of these compounds was confirmed by means of natural bond orbital (NBO) and quantum theory of atoms in molecules analyses (QTAIM). Furthermore, by applying the polarized continuum model(PCM) at the B3LYP/6-311++G(d,p) level, the pKa value of NSAIDs in aqueous solution was calculated. The maximum error was found to be less than 0.1 pKa unit in comparison with the experimental value. This protocol can be used as a tool to predict pKa values of NSAIDs in future studies. In the last step, attempts have been made to generate a functional model of the structure of human COX-2 enzyme by means of homology modeling to gain more insight into the nature of interactions between NSAIDs and the active site of this COX-2 enzyme by docking studies. In addition, a mean binding energy for each drug was estimated based on its ionization ratio.

کلمات کلیدی:

Cyclooxygenase-2 inhibitors, DFT calculations, Docking studies, Homology modeling, pKa